

# The Science of **DESIRE** New Discoveries in HSDD



## Female Sexual Dysfunction and Hypoactive Sexual Desire Disorder Background Information

1. What is Female Sexual Dysfunction?
2. What is Hypoactive Sexual Desire Disorder?
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### 1. What is Female Sexual Dysfunction?

Female sexual dysfunction (FSD) is often described as a disturbance in sexual functioning.<sup>1</sup> It is multi-dimensional and can be caused by physiological, psychological, emotional and/or relational factors.<sup>2</sup> FSD can have a major impact on a woman's sexual relationships, quality of life, interpersonal relationships and general wellbeing.<sup>3</sup>

There are four main types of FSD. According to the American Psychiatric Association's Diagnostic & Statistical Manual of Mental Disorders 4th edition (DSM-IV TR) and the World Health Organisation's International Classifications of Diseases-10 (ICD-10), FSD has been classified into the following categories:<sup>4,5</sup>

FEMALE SEXUAL DYSFUNCTION			
Sexual Desire Disorders	Female Sexual Arousal Disorder (FSAD)	Female Orgasmic Disorder (FOD)	Sexual Pain Disorders
<ul style="list-style-type: none"> <li>• Hypoactive Sexual Desire Disorder (HSDD)</li> <li>• Sexual Aversion Disorder</li> </ul>			<ul style="list-style-type: none"> <li>• Dyspareunia</li> <li>• Vaginismus</li> </ul>
<p><b>Symptoms of HSDD:</b></p> <ul style="list-style-type: none"> <li>• Lack or absence of sexual fantasies or desire for any form of sexual activity which causes marked distress or interpersonal difficulty</li> </ul> <p><b>Symptoms of Sexual Aversion Disorder:</b></p> <ul style="list-style-type: none"> <li>• Persistent and recurrent extreme aversion to and avoidance of genital sexual contact with a sexual partner</li> </ul>	<p><b>Symptoms:</b></p> <p>Persistent inability to attain or maintain sexual excitement (lubrication) adequate for the completion of sexual activity which causes marked distress and may cause interpersonal difficulty</p>	<p><b>Symptoms:</b></p> <p>Persistent or recurrent inability to have an orgasm (climax or sexual release) after adequate sexual arousal and sexual stimulation which causes marked distress and may cause interpersonal difficulty</p>	<p><b>Symptoms:</b></p> <ul style="list-style-type: none"> <li>• Recurrent or persistent genital pain associated with sexual intercourse</li> <li>• Recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with sexual intercourse</li> <li>• Sexual pain disorders cause marked distress and may cause interpersonal difficulty</li> </ul>

## 2. What is Hypoactive Sexual Desire Disorder?

Generalised, acquired Hypoactive Sexual Desire Disorder (HSDD) is a medical condition which can affect women of any age. It is characterised by a decrease in sexual desire that causes marked personal distress and/or interpersonal difficulty which cannot be exclusively attributed to another medical condition or the physiological effects of a medication.<sup>4</sup> ‘Generalised’ means that it is not dependent on a specific situation or relationship and ‘acquired’ means the condition has developed only after a period of normal sexual functioning.<sup>4</sup>

HSDD is known to be the most common form of FSD<sup>2</sup> and according to DSM-IV-TR is defined as:<sup>4</sup>

*“The persistent lack (or absence) of sexual fantasies or desire for any form of sexual activity marked by distress or interpersonal difficulty and not better accounted for by another disorder (except another sexual dysfunction) direct physiological effects of a substance (including medications) or a general medical condition”.*<sup>4</sup>

HSDD is a multi-dimensional condition that can be caused by a number of factors. Women who have HSDD often lack responsive desire and the ability to feel sexual desire when stimulated by a partner.

Women with generalised, acquired HSDD are distressed or upset because they are experiencing a decrease in their sexual desire or interest compared to what they previously experienced. They often describe the effect the condition has on them using terms including “missing something”, “concerned”, “bothered”, “frustrated”, and “discontented”.<sup>6</sup> While HSDD is the term used by specialists, it is not generally recognised by women who have this condition or physicians who are not experts in the field of sexual health.

The presence of distress or interpersonal difficulty is an integral part of HSDD and is central to the diagnosis of the condition.<sup>4</sup> HSDD can have a detrimental effect, not only on women’s sexual health, but on their quality of life and overall wellness as there is a strong correlation between sexual and general health.<sup>7,8</sup>

## 3. What is the prevalence of HSDD?

Approximately 1 in 10 women reported low sexual desire with associated distress, which may be HSDD.<sup>†9</sup> Low sexual desire with associated distress is the most commonly reported female sexual complaint. Sexual desire disorders can affect women of all ages and at any stage of their adult life.

PRESIDE<sup>9</sup> and WISHeS<sup>10</sup> are large population-based studies that analysed the prevalence of FSD, including low sexual desire with associated distress, and revealed comparable data across the US and Europe.

<sup>†</sup> The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, defines HSDD as the persistent lack (or absence) of sexual fantasies or desire for any form of sexual activity marked by distress or interpersonal difficulty and not better accounted for by another disorder (except another sexual dysfunction), direct physiological effects of a substance (including medications) or a general medical condition.

### ***The Prevalence Of Female Sexual Problems Associated With Distress And Determinants Of Treatment Seeking (PRESIDE)***

The PRESIDE study was conducted in 2006 and is the largest study of its kind. It involved more than 31,000 women aged over 18 in the US. The study investigated the prevalence of self-reported sexual problems related to desire, arousal, orgasm, and sexually-related personal distress; the combination of these problems; and the identification of associated factors.<sup>9</sup>

#### **Key findings from the PRESIDE study revealed:<sup>9</sup>**

- Approximately 1 in 10 women reported low desire with associated distress, which may be HSDD<sup>4,9‡</sup>
- Low sexual desire with associated distress was the most commonly reported female sexual complaint
- Women between the ages of 35-64 were more likely to experience distressing low desire problems than those older or younger

### ***The Women's International Study of Health and Sexuality (WISHeS)***

The WISHeS Study was conducted between 1999-2000 and involved over 3,500 women (1,591 from the US and 1,998 from Western Europe) between the ages of 20-70.<sup>10</sup>

#### **Key findings from the WISHeS study revealed:<sup>10</sup>**

- The prevalence of HSDD ranged from 6-13% in Europe and 12-19% in the US
- In Europe, the proportion of women with low desire increased significantly with age, however older women suffered less from associated distress compared to younger women
- In the US there was no significant trend toward an age-related increase in the proportion of women with low desire
- However, as seen in Europe, women from the US between the ages of 60-70 suffered less from low desire with associated distress than women in their middle ages and twenties

## **4. How is HSDD diagnosed?**

Historically, accurate diagnosis of HSDD required an extensive standard diagnostic interview administered by a specialist clinician, which can take up to one hour.<sup>11</sup> The interview determines whether low desire could be caused by another medical condition unrelated to HSDD. Diagnosis by a gynaecologist or health care practitioner, not necessarily trained in FSD, is often hindered due to a number of factors; time constraints during initial consultation; doctor or patient embarrassment discussing issues related to sex; a lack of physician experience in diagnosing the condition; a lack of referral services/specialists; and limited availability of treatment options.<sup>2</sup>

To help facilitate the dialogue about sexual health and aid physicians in diagnosing HSDD, a diagnostic tool, called the Decreased Sexual Desire Screener (DSDS), has been developed. The tool consists of five yes or no questions and can assist clinicians, including experts in Sexual

<sup>‡</sup> The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, defines HSDD as the persistent lack (or absence) of sexual fantasies or desire for any form of sexual activity marked by distress or interpersonal difficulty and not better accounted for by another disorder (except another sexual dysfunction), direct physiological effects of a substance (including medications) or a general medical condition.

Medicine as well as non-experts to diagnose the condition with high accuracy.<sup>12</sup> The DSDS also allows the identification of women who do not have HSDD but may be experiencing low sexual desire due to secondary causes such as other medical conditions which, according to the DSM-IV, do not constitute HSDD.<sup>4,12</sup> The DSDS is a validated tool and follows the recommendation from the US Food and Drug Administration (FDA), which notes that new diagnostic instruments should be developed in order to distinguish between patients with FSD, or a specific component of FSD, and those without FSD.<sup>13</sup>

The DSDS may also help to facilitate a conversation between a physician and patient on a topic that is often regarded as uncomfortable to discuss. Results from the PRESIDE study highlighted the difficulty in conversations between patients and physicians about HSDD and the study revealed the following key insights:<sup>14</sup>

- More than 60% of women with HSDD do not seek information from a health professional. In fact, most women have never discussed their sexual problems with a healthcare professional preferring instead to seek information from a friend or spouse, or anonymous sources such as television, radio or the internet<sup>14</sup>
- Sexual problems were most often first discussed during a routine examination (58%) or an appointment for other conditions (33%)<sup>14</sup>
- In nearly half of the cases (47%), gynaecologists were the first HCPs with whom women discussed their sexual problems, followed by primary care physicians (39%)<sup>14</sup>
- Two thirds of women (66%) indicated that they had never received any treatment for their sexual problems<sup>14</sup>

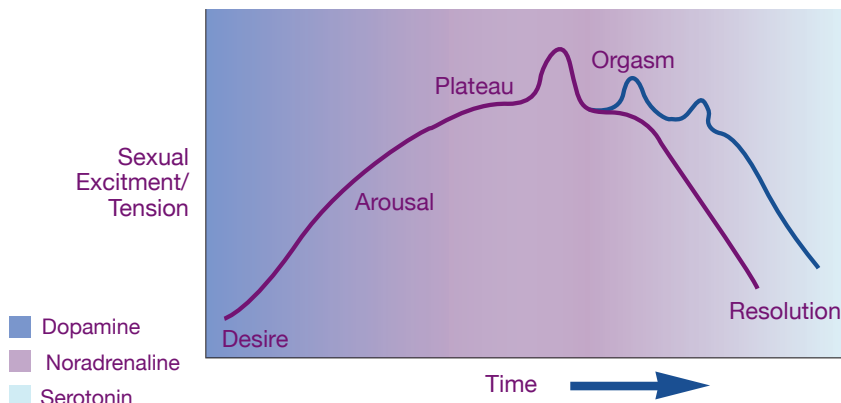
## 5. What causes HSDD?

There are a number of potential causes and contributing factors to HSDD that have been identified reflecting a complex interaction of physiological, psychological, emotional and/or relationship components.<sup>2</sup>

The imbalance of neurotransmitters is thought to be one of several factors that can impact sexual function and cause HSDD. Relationship problems, poor body image, decreased self-esteem, an imbalance of sex hormones (androgens, oestrogen, progesterone) can also contribute to a decrease in sexual desire.<sup>15</sup> This highlights the complex nature of sexual function and the manifestation of sexual dysfunction including HSDD.<sup>2</sup> A thorough understanding of the complex interaction between all these factors is needed in order to identify and help women with this condition.<sup>12</sup>

The sexual response cycle involves phases of sexual desire, sexual arousal, orgasm and resolution (characterised as the sense of muscular relaxation and general well-being).<sup>16,17</sup> See figure 1.

**Figure 1**  
Female Sexual Response Cycle<sup>16,17</sup>



It is widely accepted that the brain is central to sexual function and plays an important role in female sexual desire.<sup>15</sup> Current medical research suggests that neurotransmitters in the brain particularly dopamine, norepinephrine and serotonin play a key role in modulating sexual desire.<sup>2,18,19,20</sup>

Sexual dysfunctions could occur when the balance of these neurotransmitters is disrupted. Diminished function of the dopamine system, which increases sexual desire and excitement, and norepinephrine system, which affects arousal and orgasm, could lead to the inability to begin the sexual response cycle. An overactive serotonin system, which can decrease desire and delay orgasm could also lead to inhibition of sexual response. If these neurotransmitter systems are not appropriately balanced, sexual dysfunction could occur. Women with HSDD may have an imbalance in these systems, which could affect the typical progression of the sexual response cycle and the ability to experience sexual desire.<sup>16,17</sup> See figures 2 and 3:

**Figure 2**  
Balance of neurotransmitter systems is necessary in the sexual response cycle:<sup>21,22</sup>

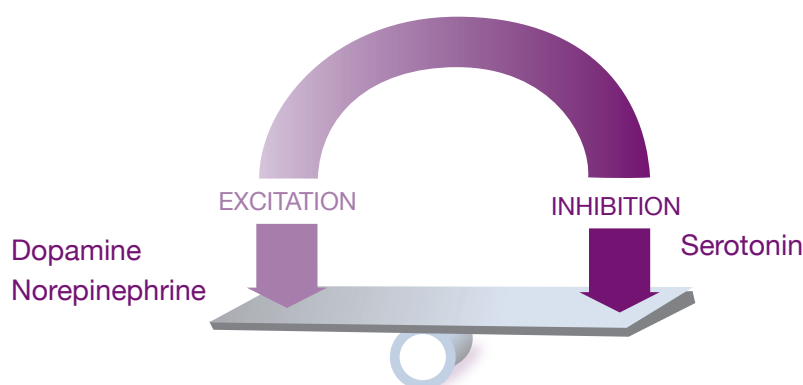
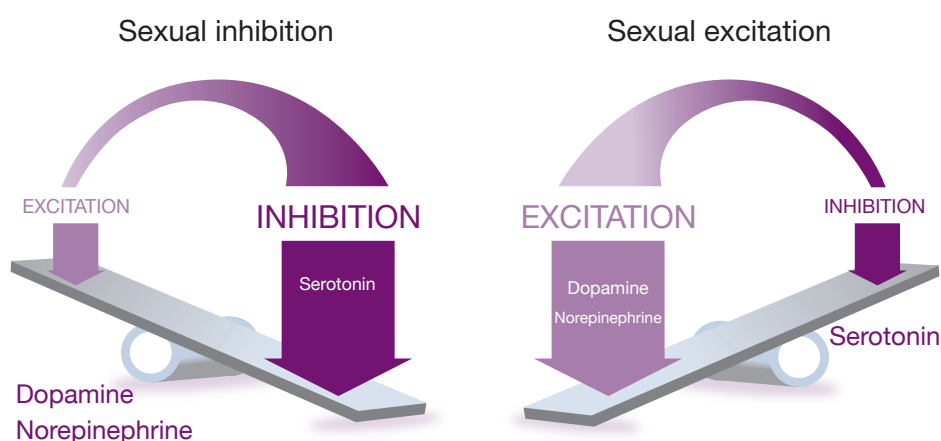


Figure 3



The figure illustrates how a relative lack of dopamine and norepinephrine and excess serotonin can inhibit the sexual response cycle. This inhibition may limit an individual's response to sexual stimuli. Natural sexual excitation and response is possible when these neurotransmitters are appropriately balanced.

## 6. How is HSDD treated?

HSDD is a complex, multi-factorial condition requiring a multi-disciplinary approach to its management and there are currently no treatments for pre-menopausal women with HSDD that meet all patients' needs. Cognitive behavioural therapy and counselling may benefit some women suffering from HSDD and a testosterone patch is approved in Europe for post-menopausal women who experience HSDD as a result of a bilateral oophorectomy and hysterectomy.<sup>24</sup> However these are not the complete answers to the needs of the many women suffering from this condition.

Given the hypothesised mechanisms of the sexual response cycle, Boehringer Ingelheim is investigating flibanserin<sup>1</sup> as a novel, non-hormonal treatment for HSDD. It is being studied as an oral daily treatment for pre-menopausal women experiencing HSDD. Unlike existing treatment options, flibanserin<sup>§</sup> is centrally-acting and has two main pharmacological targets in the brain: 5-HT<sub>1A</sub> receptors (agonism) and 5-HT<sub>2A</sub> receptors (antagonism). Flibanserin<sup>§</sup> targets these receptors preferentially in selective brain areas and the mode of action is under investigation. What Boehringer Ingelheim have learned from pre-clinical research so far suggests that binding of flibanserin to its receptors in selective regions of the brain affects the neurotransmitters dopamine, norepinephrine and serotonin which play a role in the healthy sexual response cycle. By modulating these neurotransmitters in selective brain areas flibanserin might help to restore a balance between inhibitory and excitatory factors which could lead to a healthier sexual response.<sup>25</sup>

### Notes to Editors

Please refer to additional background information documents for further information on flibanserin<sup>§</sup> and Boehringer Ingelheim's Bouquet<sup>®</sup> Study Programme.

<sup>§</sup>This compound is an investigational agent. Its safety and efficacy have not yet been fully established.

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